

REMARKS

Claims 1, 2, 7, and 62-64 have been amended. Claim 65 is new. Claims 5 and 6 have been canceled. Claims 8-61 are withdrawn. Claims 1 and 7 have been amended to incorporate the limitations of claim 5 and 6. Claims 1 and 7 have also been amended to replace the term "binds to an antibody having the binding specificity of HECA-452" with the term "comprises HECA-452 reactive sialylated, fucosylated N-glycans". Support for this amendment can be found, e.g., at page 2, lines 7-9, of the specification. Claims 1 and 62-64 have been amended to delete the words "a" and "isoform" flanking the words "human CD44H", "human CD44R1", and "human CD44R2". Claims 1 and 7 have been amended to require that the preparations comprise less than 5% of a polypeptide other than the glycosylated CD44 polypeptide. This amendment is supported, e.g., at page 11, lines 13-27, of the specification. Claim 2 has been amended to correct a typographical error. Support for new claim 65 can be found, e.g., at page 2, lines 7-9, of the specification. No new matter has been added.

Rejections Under 35 U.S.C. § 112, First Paragraph (Written Description)

Claims 1-7 and 62-64 were rejected as lacking written description. This rejection is traversed. The claims, as amended, are drawn to preparations of a purified glycosylated CD44 polypeptide having several structural limitations. For example, the glycosylated CD44 polypeptide of claim 1 includes specified exons of human CD44, for example, the CD44 polypeptide is human CD44H, human CD44R1, or human CD44R2. In addition, the polypeptide has to be glycosylated such that it is HECA-452 reactive, i.e., it binds to an antibody having the binding specificity of monoclonal antibody HECA-452. Thus, the claimed glycoprotein has a combination of art-known elements, i.e., a polypeptide backbone of CD44, e.g., human CD44H, human CD44R1 or human CD44R2, and a carbohydrate structure that is reactive with antibodies having the specificity of monoclonal antibody HECA-452. The identifying characteristic feature of claimed polypeptides is a combination of these art-known elements in a new way, namely a CD44 polypeptide glycosylated such that it binds a monoclonal antibody having the binding specificity of monoclonal antibody HECA-452. Applicant discovered that this unique

combination of elements provides a version of CD44 that binds E-selectin and L-selectin. As discussed below, each of the elements to be combined was known, separately, in the art. By naming and pointing to these known elements, the Applicant has demonstrated possession of them for use in the claimed invention.

With regard to the structural limitation that the claimed polypeptides are glycosylated such that they are reactive with monoclonal antibody HECA-452, the Examiner alleges that the claims are not adequately described because they refer to the binding specificity of HECA-452, yet HECA-452 binding activity is not restricted to CD44 polypeptides. The Examiner's repetition of this point is not understood.

As discussed above, the Applicant has discovered a novel combination of elements, namely CD44 polypeptide backbones that are glycosylated such that they bind monoclonal antibodies having the binding specificity of HECA-452. Thus, the claims require that the purified glycosylated polypeptides be CD44 polypeptides **AND** that they bind to an antibody having the binding specificity of HECA-452. The fact that HECA-452 binds epitopes expressed on other polypeptide backbones is irrelevant to the issue of description of the present claims. Instead, the Examiner's statements reiterate Applicant's position that sialofucosylated carbohydrate epitopes reactive with HECA-452 were known, just not in combination with a CD44 polypeptide as currently claimed. Thus, just naming this structural property of the claimed glycosylated polypeptide is sufficient to adequately show possession of this portion of the claimed combination.

Furthermore, by naming the various CD44 polypeptides that form the polypeptide backbone of the glycosylated polypeptide, the Applicant has also provided sufficient description of this structural element of the claims. Many of the claims specifically state that the CD44 polypeptide portion of the glycosylated polypeptide is human CD44H, human CD44R1 or human CD44R2. The Examiner stated that "[a]lthough page 10, paragraph 3 of the specification discloses a CD44R1 and CD44R2 isoform, the actual structure of said CD44R2 isoform is not readily apparent. Further, applicant has not provided a sufficient number of species to support a genus of CD44R1 and CD44R2 isoforms." First, Applicant notes that claim 1 has been amended

to recite “human CD44H”, “human CD44R1” and “human CD44R2”. Second, the Examiner’s position is inconsistent with that of the MPEP and the Court of Appeals for the Federal Circuit. Applicant has clearly disclosed isoforms that are encompassed by the claims. Sequences of human CD44H, CD44R1, and CD44R2 are known. See, e.g., Dougherty et al., *J. Exp. Med.*, 174:1-5 (1991). Furthermore, it is Applicant’s position that many versions of human CD44 (including CD44H, CD44R1, and CD44R2) were known at the time of filing. It was also known that the sites needed for N-linked glycosylation of CD44 occur within the first few exons of CD44. See, e.g., Bartolazzi et al. *J. Cell Biol.*, 132(6):1199-1208 (1996), submitted herewith as Exhibit A. Because the amino acid sequences of human CD44 polypeptides (including those portions necessary for glycosylation) were well known in the art at the time of filings, just naming these polypeptides is sufficient to provide adequate description.

It is important to understand what the invention is and what it is not. The discovery is not a new genetic sequence, as it was in the *Amgen* and *Lilly* cases cited by the Examiner. The identifying characteristic of the claimed polypeptides is not a novel polypeptide sequence. Rather, Applicant is claiming a novel combination of a CD44 polypeptide glycosylated such that it reactive with monoclonal antibody HECA 452 and this combination is sufficiently described in the specification for the purposes of the claims. In view of what is being claimed, Applicant submits that the Examiner’s reliance on cases such *Amgen*, *Eli Lilly* and *Fiers* and statements such as “the description of a genus is achieved by recitation of a representative number of DNA molecules, defined by nucleic acid sequence, falling within the scope of the genus” is inappropriate. None of these cases concerned situations in which the relevant sequences were described in the prior art.

Instead, cases such as *Capon v. Eshhar* (418 F.3d 1349, 76 U.S.P.Q.2d 1078 (Fed. Cir. 2005) and *Falkner v. Inglis* (2006 WL 1453040 (Fed. Cir. 2006)) are more appropriate for claims covering a new combination of art known elements which result in CD44 polypeptides that have a new property, i.e., the ability to bind E-selectin and L-selectin. The Federal Circuit has repeatedly held that a patent applicant need not re-describe sequence information in his patent application to meet the written description requirement when the sequence information is in the

prior art. In *Capon*, the court reversed the Board of Patent Appeals and Interferences' and found that the written description requirement was met where a patent specification named but did not reiterate the structure or formula or chemical name of sequences known in the art. In *Falkner*, the court noted that there is no "*per se* rule that whenever a claim limitation is directed to a macromolecular sequence, the specification must always recite the gene or sequence, regardless of whether it is known in the prior art." The court stated that "the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification." The *Falkner* court held that, where accessible literature sources clearly provided sequence information as of the relevant date, satisfaction of the written description requirement does not require either the recitation or incorporation by reference of sequences. Similarly, in the present application, merely naming human CD44 polypeptides including specific isoforms, where accessible literature clearly provides the sequence information as of the filing date, is sufficient to describe the CD44 polypeptide portion of the glycosylated polypeptide.

The Examiner has repeatedly ignored that the claimed glycosylated polypeptides are a combination of elements. For example, the Examiner stated that

while applicant appears to rely on known or 'standard or hematopoietic isoforms of CD44' applicant continues to try to distinguish the instantly claimed HCELL from other known CD44 glycoforms without necessarily claiming those distinguishing structural characteristics that are correlated to the particular functionals [sic] characteristics now claimed, other than the limited species disclosed in the specification as filed.

Applicant disagrees. Applicant again reiterates that the fact that the claimed forms of glycosylated CD44 polypeptides bind to an antibody having the binding specificity of HECA-452 IS a distinguishing structural characteristic, and it is coupled with the requirement that the polypeptides include a CD44 polypeptide backbone. Furthermore, the requirement that the polypeptides bind to an antibody having the binding specificity of HECA-452 is a distinguishing structural characteristic that is correlated to particular functional characteristics. The correlation between HECA-452 reactivity and functional characteristics is clearly set forth in the specification. See, e.g., page 9, lines 4-6, which indicates that that L-selectin and E-selectin

ligand activity requires glycans that are recognized by rat monoclonal antibody HECA-452. HECA-452 reactivity is a structural requirement and it correlates with function of the claimed polypeptides.

The amendments to claim 1 and the addition of claim 65 better clarify both the scope of the present invention and the distinction between the invention and other CD44 glycoproteins previously known in the art.

In view of the foregoing, Applicant requests that the rejection for lack of written description be withdrawn.

Rejections Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1-7 and 62-64 were rejected as lacking enablement for the claimed compositions. This rejection is traversed.

Claim 1 and its dependent claims are directed to purified preparations of glycosylated CD44 polypeptides, wherein the CD44 polypeptide is human CD44H, human CD44R1, or human CD44R2. Claim 7 is directed to a purified preparation of a glycosylated polypeptide comprising the amino acid sequence of SEQ ID NO:1. The claimed preparations also require that the polypeptides bind to an antibody having the binding specificity of HECA-452.

In applying this rejection, the Examiner argued that "it is maintained that the current claims are broader in scope than the particular KG1a/CD44H/CD44R2 CD44 isoforms that are disclosed in the specification which are asserted to be distinguishable from the prior art CD44 isoforms." Applicants believe that the claims already provided such a distinction and were commensurate in scope with the HCELL disclosed in the application. However, in order to better clarify the differences between the claimed glycopolypeptides and prior art CD44 glycoforms, applicants have amended claim 1 and added claim 65. If the Examiner intends to maintain this rejection over these amended claim, Applicant has misunderstood the rejection and requests that the Examiner clarify what is meant by his statement.

The amended and added claims clearly state which forms of human CD44 are encompassed in the preparations. Specifically, amended claim 1 and its dependent claims require that the polypeptide have a polypeptide backbone of CD44, such as CD44H, CD44R1, or CD44R2. These polypeptides are glycosylated such that they possess sialylated, fucosylated N-glycans that are reactive with monoclonal antibody HECA-452. Amended claim 1 also requires that the glycosylated polypeptide be a ligand for both an E-selectin and L-selectin. It is not understood why the isoforms recited in the claims were perceived by the Examiner to be broader than the isoforms disclosed in the specification, but the amended claims eliminate any such perception. Applicant notes that claim 1 and its dependent claim have also been amended to refer to human CD44H, human CD44R1, and human CD44R2 rather than "a CD44H isoform", etc.

Added claim 65 recites that the glycopolypeptide of the invention is "a hematopoietic cell E-selectin/L-selectin ligand (HCELL) polypeptide, wherein said HCELL polypeptide is a glycoform of CD44 that comprises HECA-452 reactive sialylated, fucosylated N-glycans, and wherein said HCELL polypeptide is a ligand for both L-selectin and an E-selectin." Characterizing the claimed glycopolypeptide as HCELL possessing the recited properties distinguishes applicant's presently claimed invention from all prior art glycoforms of CD44.

The Examiner also argued that the claims are not enabled because they do not recite specific sequences. As discussed above with respect to written description, Applicant is not required to recite known sequences in the specification. There is no reason to conclude that one would need undue experimentation to make and use a polypeptide preparation on the basis that the polypeptide sequence is not explicitly recited, even though the polypeptide sequence is known. For enablement, the knowledge of the skill in the art as well as the guidance in the application must be considered. Here, the claims recite polypeptide backbones that have sequences known in the art. Furthermore, all of the polypeptides recited in the claims were known to include all 5 N-linked glycosylation sites of CD44. In view of such knowledge in the art, specific recitation of amino acid sequence of the polypeptides in the application is not necessary to enable the claimed invention.

The purpose of the enablement requirement is to ensure that the patent specification teaches one of skill in the art to make and use the claimed invention. The Examiner urged that the claims are not enabled because there is insufficient guidance for making and using a genus of compositions encompassed by the claims. According to the Examiner,

[b]ecause of the lack of sufficient guidance and predictability in determining which structures would lead to the identification of the featured KG1a/CD44H/CD44R1/CD44R2 CD44 isoforms of the instant invention and asserted to be distinguishable from other CD44 isoforms with the disclosed properties and the relationship between the critical distinguishing structural elements of said KG1a/CD44H/CD44R1/CD44R2 CD44 isoforms was not well understood and was not predictable, it would require an undue amount of experimentation for one of skill in the art to arrive a [sic] genus of the instant featured KG1a/CD44H/CD44R1/CD44R2 CD44 isoforms that are distinguishable from other CD44 isoforms. The instant specification provides a starting point from which one of skill in the art can perform further research in order to practice the claimed invention, but this is not adequate to constitute enablement in that will [sic] enable any person skilled in the art to make and use the invention.

The Examiner concludes that the relationship between the distinguishing structural elements of the claimed compositions was not well understood without considering the nature of the claims and the disclosure of the specification. The amended and added claims make clear this relationship by requiring that the preparations include a purified CD44 glycoform that contains HECA-452 reactive sialylated, fucosylated N-glycans, is a ligand for both an E-selectin and L-selectin, and comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide, including non-HECA-452 reactive CD44 isoforms and other non-CD44 HECA-452 reactive glycoproteins. The specification teaches one of skill in the art to make and use such preparations without undue experimentation. Methods for identifying polypeptides that fall within the claims, e.g., by employing anti-CD44 and HECA-452 antibodies, are disclosed, e.g., in Example 4 at pages 42-45 of the specification. Expression of CD44 polypeptides and purification of the polypeptides, is described in the specification and/or is known (see, e.g., page 26, line 21, to page 27, line 20, describing expression of nucleic acids encoding CD44 and glycosyltransferases).

Lastly, determining whether a CD44 polypeptide is HECA-452 reactive does not require undue experimentation. In fact, the Examiner has acknowledged that Applicants have taught how to make and use at least one isoform having this property. The Examiner's contention that there is a lack of predictability "in determining which structures would lead to the identification of the featured KG1a/CD44H/ CD44R1/CD44R2 CD44 isoforms" has no basis in light of the claim amendments.

In view of the foregoing, Applicant requests that the rejection of claims 1-7 and 62-64 as lacking enablement be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph (Indefiniteness)

Claims 1-7 and 62-64 were rejected as indefinite for failing to particularly point out and distinctly claim the subject matter Applicant regards as the invention. This rejection is traversed.

As amended, the claims 1-6 and 62-64 are drawn to preparations including CD44H, CD44R2, and CD44R1. It is believed that the amendment to the claims obviates this rejection. As noted in the previous reply, the terms "CD44H", "CD44R1", and "CD44R2" are not arbitrary protein names but are names of specific isoforms. CD44H is described in detail at page 9, lines 15-31. The specification provides that this isoform is encoded by exons 1-5, 16-18, and 20 of a CD44 gene (page 9, lines 18-20). The open reading frame includes 1482 base pairs of mRNA and translates into a polypeptide chain of approximately 37 kDa (prior to modification by glycosylation)(page 9, lines 22-24). The approximate number of amino acids in each domain is also noted (page 9, lines 26-28). Because the amino acid sequence of CD44H is known and that detailed structure of the isoform is characterized in the specification, the term "CD44H" as used in the claim is definite. Applicant also notes that the entire sequence of the CD44H isoform is contained within CD44R1 (SEQ ID NO:1). CD44R1 differs from CD44H by the insertion of a 132 amino acid region corresponding to residues 223-355 of SEQ ID NO:1 (see Dougherty et al., *J. Exp. Med.*, 174:1-5, 1991). The term "CD44R2" is similarly definite. As is known in the art, CD44R2 differs from CD44H by the presence of an insertion of an amino acid sequence. The entire sequence of CD44R2 is contained within SEQ ID NO:1. CD44R2 differs from SEQ ID

NO:1 in that it lacks amino acids 224-293 of SEQ ID NO:1 (see Dougherty et al., *J. Exp. Med.*, 174:1-5, 1991). Applicant submits that the terms "CD44H", "CD44R1", and "CD44R2" are definite as used in claims.

The Examiner included claim 7 in the rejection. Claim 7 is directed to a purified preparation of a glycosylated polypeptide comprising the amino acid sequence of SEQ ID NO: 1, wherein said glycosylated polypeptide binds to an antibody having the binding specificity of monoclonal antibody HECA-452, and wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated polypeptide. None of the stated grounds for rejection appear to apply to this claim.

In view of the foregoing, withdrawal of the rejection of claims 1-7 and 62-64 as indefinite is requested.

Rejections Under 35 U.S.C. § 102

Dimitroff et al.

Claims 1-7 and 62-64 were rejected under 35 U.S.C. § 102(a) as anticipated by Dimitroff et al. (*Proc. Natl. Acad. Sci.*, 97(25):13841-13846, 2000); "Dimitroff"). A reference is citable as prior art under 35 U.S.C. § 102(a) if it was described in a printed publication before the date of invention by the applicant for a patent. Dimitroff was published online on November 28, 2000, and was published in print on December 5, 2000. The present application claims the benefit of priority of U.S.S.N. 60/240,987, filed on October 18, 2000. Dimitroff was published after the filing date of U.S.S.N. 60/240,987, and therefore is not citable under 35 U.S.C. § 102(a). Withdrawal of this rejection is requested.

Sackstein et al.

Claims 1-7 and 62-64 were rejected as anticipated by Sackstein et al. (*Blood*, 89:2773-2781, 1997; "Sackstein") as further evidenced by Dimitroff et al. (*J. Biol. Chem.*, 276:47623-47631, 2001; "Dimitroff") and Sackstein (*J. Invest. Dermatol.*, 122:1061-1069, 2004; "Sackstein 2"). This is respectfully traversed.

The Examiner stated that “[i]t is the inventor Sackstein who teaches the hematopoietic cell L-selectin ligand which exhibits sulfate-independent binding activity that appears to be the same KG1a CD44 glycosylated polypeptide of the claimed invention.” The Examiner also stated, in response to Applicant’s arguments, that “[i]t appears that applicant is simply asserting that Sackstein does not state the claimed limitations, yet provides no objective evidence that this prior art by the inventor Sackstein teaching the same HCELL somehow is different from that claimed and disclosed in the instant application.”

The claims are directed to purified preparations of a glycosylated CD44 polypeptide, wherein the glycosylated CD44 polypeptide binds to an antibody having the binding specificity of monoclonal antibody HECA-452, and wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide.

The Examiner argued that Sackstein anticipates the claims because Sackstein describes an L-selectin ligand which exhibits certain functional properties later found to be attributable to particular glycoforms of CD44. Applicant has noted in the previous responses that Sackstein does not describe any purified glycosylated CD44 polypeptides, which is explicitly required by the claims. A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. Applicant requests that the Examiner consider the fact that no purified glycosylated CD44 polypeptide preparations are described in the cited reference, as this point has not been noted or addressed by the Examiner. The ligand described by Sackstein was characterized by functional assays. Regardless of the identity of the ligand, no purified preparations of glycosylated CD44 polypeptides were described by Sackstein.

Sackstein first describes experiments which show that incubation of KG1a cells with a monoclonal antibody that recognizes sulfate-dependent epitopes, MECA79, does not inhibit adherence of KG1a cells to lymphocytes (Sackstein, page 2777, right col.). Sackstein next states that MECA79 does not bind to KG1a cells (Sackstein, page 2778, left. col., and Figure 1). Sackstein presents immunoprecipitations from radiolabelled KG1a cell lysates which show that MECA79-reactive polypeptides were not precipitated from KG1a lysates whereas another

polypeptide, CD43, was precipitated from the lysates (Sackstein, Figure 2 and page 2778, right col.). Sackstein further reports the results of experiments in which KG1a cells were treated with neuraminidase to remove sialylated moieties from the cells, and cells were incubated in the presence and absence of chlorate, cycloheximide, or tunicamycin to determine whether the inhibitors blocked re-appearance of L-selectin ligand activity after neuraminidase treatment (Sackstein, pages 2778-2779). None of the experiments in Sackstein report the isolation of a preparation of purified CD44 glycoproteins. The other references cited by the Examiner as extrinsic evidence of anticipation (i.e., Dimitroff and Sackstein 2) do not change this fact.

The Examiner cited *In re Spada* (911 F.2d 705, 15 U.S.P.Q.2d 1655 (Fed. Cir. 1990)) for the proposition that products of identical chemical composition cannot have mutually exclusive properties. As discussed above, Sackstein does not describe a preparation of identical chemical composition to that of the present claims. Sackstein does not describe any purified preparations of glycosylated CD44 polypeptides. The Examiner cited *In re Schreiber* (128 F.3d 1473, 44 U.S.P.Q.2d 1429 (Fed. Cir. 1997)) for the proposition that the Patent Office has the authority to require the applicant to prove that the subject matter shown in the prior art does not possess the characteristics relied on. *In re Schreiber* is inapplicable, for the claims require a purified preparation of glycosylated CD44 polypeptides. No such preparations are disclosed in Sackstein. Applicant is not relying on a characteristic, the presence or absence of which is unclear from reading the Sackstein reference. The Examiner also cited *Atlas Powder Co. v. Ireco* (190 F.3d 1342, 51 U.S.P.Q.2d 1943 (Fed. Cir. 1999)) for the proposition that the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. This aspect of *Atlas Powder* is also inapplicable to the present case, in part, because a high level of purity of a glycosylated CD44 preparation is not inherent in a composition described in the cited reference. In *Atlas Powder*, it is noted that when a patent claims a chemical composition in terms of ranges of elements, any single prior art reference that falls within each of the ranges anticipates the claim. 190 F.3d at 1346. There is no composition described in Sackstein which is sufficiently enriched for the requisite glycosylated CD44 polypeptides to satisfy the limitations

of the present claims. In view of the foregoing, Applicant requests that the Examiner withdraw the rejection of claims 1-7 and 62-64 as anticipated by Sackstein.

Stamenkovic et al.

Claims 1-7 and 62-64 were rejected as anticipated by Stamenkovic et al. (*EMBO J.*, 10:343-348, 1991; "Stamenkovic") as evidenced by Sackstein (U.S. Pat. Pub. No. 2003/0040607; "US 2003/0040607") and Sackstein 2. The Examiner stated that "Stamenkovic et al. teach the expression of CD44 transcripts in primary tumors of mesenchymal and epithelial origin, in normal epithelium and in lymphocytes (see page 344, column 1, paragraph 1 and Figure 2 as well as pages 345-346)." This rejection is traversed.

The Examiner referred to Figure 2 and pages 344-345 of Stamenkovic as evidence of anticipation. Figure 2 shows CD44 transcripts (i.e., RNA) from various cell types. The claims are drawn to purified preparations of glycosylated CD44 polypeptides. Figure 2 of Stamenkovic is a photo of an RNA blot and does not indicate that particular glycoforms of CD44 polypeptides were isolated. It does not even indicate that CD44 polypeptides were expressed in the cell lines analyzed. The claims require highly purified preparations of CD44 polypeptides which are glycosylated such that they bind to an antibody having the binding specificity of HECA-452. Stamenkovic did not identify or purify any particular glycoforms of CD44, much less CD44H, CD44R1, or CD44R2, which bind to an antibody having the binding specificity of HECA-452.

The Examiner cited Sackstein 2 as evidence that the claims lack novelty. In Sackstein 2, it states:

Although initially considered to be a 'novel' selectin ligand by the above biochemical criteria, mass spectrometry subsequently revealed that HCELL is not novel *per se*: it is a glycoform of a well-recognized integral membrane glycoprotein, CD44, that expresses the CLA epitope (i.e., is recognized by mAb HECA-452).

Contrary to the Examiner's arguments, this discussion of HCELL in Sackstein 2 does not provide evidence that the claims are anticipated by Stamenkovic. The present inventor used mass spectrometry to determine the identity of the polypeptide responsible for the observed

selectin ligand activity and discovered that the polypeptide backbone was that of CD44. The fact that the polypeptide backbone was not a novel polypeptide backbone does not mean that the claims lack novelty. The statement above merely acknowledges that the identity of the backbone was CD44 rather than some previously-undiscovered polypeptide backbone. It does not demonstrate that a CD44 polypeptide having a particular carbohydrate structure that is reactive with monoclonal antibody HECA-452 was not novel. Nothing in Sackstein 2 shows that Stamenkovic's disclosure anticipates the present claims. To serve as an anticipation when a reference is silent about an inherent characteristic, an extrinsic reference may be cited and it must make clear that the missing descriptive matter was necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. See *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1268 (Fed. Cir. 1991). Sackstein 2 does not, and cannot, show that Stamenkovic describes a preparation of a purified glycosylated CD44 polypeptide which binds to an antibody having the binding specificity of monoclonal antibody HECA-452, wherein the preparation comprises less than 5% of a polypeptide other than the glycosylated CD44 polypeptide, because no such preparation was made by Stamenkovic.

For the reasons provided above, Applicant respectfully requests that this rejection be withdrawn.

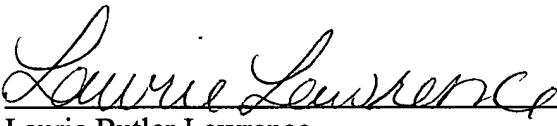
Applicant : Robert Sackstein
Serial No. : 10/042,421
Filed : October 18, 2001
Page : 25 of 25

Attorney's Docket No.: 10286-014001 / BWH-729

Enclosed is a check for the Petition for Extension of Time fee. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: 10/16/01


Laurie Butler Lawrence
Reg. No. 46,593

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

21358967.doc